54. (New) A substrate according to Claim 1, wherein the coating is deposited using a precursor selected from the group consisting of tetrametylsilane, trimetylsilane, tetramethoxysilane, heamethyl disilane, hexamethyl disiloxane, hexamethyl disilazane, methane, ethane, ethylene, tetraalkoxy titanates, and combinations of the above.

Remarks

Claims 1-20 are pending in the application, Claims 33-43 having been withdrawn in response to the Examiner's restriction requirement. Claims 21-32 have been canceled. Claims 44-54 are new.

Claims 1-32 stand rejected under 35 U.S.C. § 112. Claims 1-30 stand rejected under 35 U.S.C. § 102(b) as being anticipated by U.S. Patent No. 5,968,745 to Thorp *et al* (hereinafter "Thorp"). Claims 31 and 32 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Thorp taken in combination with U.S. Patent No. 5,632,957 to Heller *et al.* (hereinafter "Heller").

I. Claim Rejections under 35 U.S.C. § 112, second paragraph

In light of the above amendments and the following remarks, Applicants respectfully request that the rejections to the claims identified in Paragraph 8 a-h of the Action be withdrawn.

Paragraph 8a states that Claim 1 allegedly does not particularly point out how the surface is "chemically modified," and that it is not clear whether the presence of the "coating" and terminal "functional group" components constitutes the chemical modification. Paragraph 8b states that the terms "base layer" and "substrate" are unclear. Accordingly, claim 1 has been amended to remove the phrase "chemically modified" and "base layer" in response to the Examiner's objection. Applicant submits that the term substrate is adequately defined in Claim 1.

Paragraph 8c states that it is unclear what is meant by the term "a chemically crosslinked material" and that it is not clear whether a "chemically crosslinked material" as defined by definitions (1)-(4) could include, for example, carbon in the form of a diamond (definition (3)). Paragraph 8c also states that it is not clear what type of "chemically crosslinked material" as defined by definition (5) could be

prepared solely from (a) carbon and oxygen, (b) carbon and nitrogen, or (c) carbon and hydrogen. Applicants respectfully submit that the term "chemically crosslinked" is well understood by those of ordinary skill in the art, and therefore the term and its definitions are clearly defined. According to McGraw-Hill's Dictionary of Scientific and Technical Terms, 3rd Ed. (1984), chemical "crosslinking" refers to "the setting up of chemical links between the molecular chains of polymers." Thus, it is clear to one of ordinary skill in the art that the chemically crosslinked material in Claim 1 is any such chemically linked molecular chain of polymers that include elements from one or more of definitions (1) – (5) in Claim 1.

Claims 3 and 17 have been amended in response to the Examiner's objections in paragraph 8g and 8h of the Action. Claims 21, 22, 31 and 32 have been deleted.

II. Claim Rejections under 35 U.S.C. § 112, first paragraph.

Claims 1-32 are rejected under 35 U.S.C. § 112, first paragraph, for lack of enablement. The Action alleges that the specification, while providing enablement for a process disclosed by example 1, does not reasonably provide enablement for the scope encompassed by the claims.

Applicants submit that the position of the Action is opposite to controlling law regarding the requirements of enablement. More specifically, Applicants respectfully submit that the Office Action has not met the burden imposed on the Patent Office in making an enablement rejection. The test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation. M.P.E.P. § 2164.01 (citing *United States v. Telectronics, Inc.*, 857 G.2d 778, 785 U.S.P.Q.2d 1217,1223 (Fed.Cir. 1988)). As discussed in the M.P.E.P., the Examiner has the initial burden to establish a reasonable basis to question the enablement provided for the claimed invention. M.P.E.P. §2164.04 (citing *In re Wright*, 999 F.2d 1557, 27 USPQ2d 1510 (Fed. Cir. 1993)) (examiner must provide a reasonable explanation as to why the scope of protection provided by a claim is not adequately enabled by the disclosure).

Paragraph 10 of the Action includes several questions regarding how the surface is made and used in a detection system and where the surface would be located in such a system. Regarding how a surface according to the invention is

made, the present application includes a description of exemplary techniques for depositing a coating according to the invention on a substrate. The exemplary techniques include Plasma Enhanced Chemical Vapor Deposition (PECVD), Chemical Vapor Deposition (CVD), sputtering, evaporation, and other deposition techniques such as plating, dip-, flow-, spray-, or spin coating. *See* Specification, Page 6, line 30 – Page 7, line 3. Further details regarding how to deposit a coating according to the invention on a substrate, including specific examples, are given on Page 7, line 3 – Page 13, line 2.. The exemplary techniques for depositing a coating on a substrate are known in the art, may be used to deposit a coating according to the invention without "undue experimentation," and therefore, do not need to be further elaborated on in the present application. According to the M.P.E.P., "[a] patent need not teach, and preferably omits, what is well known in the art." M.P.E.P. 2164.01(a) (citing, *e.g.*, *In re Cuchner*, 929 F.2d 660, 661, 18 U.S.P.Q.2d 1331, 1332 (Fed.Cir. 1991)).

Turning now to how a surface according to the invention is used, Applicants submit that the present application discloses how a coating according to the invention could be used, specifically, in a detection device. In an exemplary detection device, biomolecules in a sample solution contained in a cell are capable of giving rise to an electrochemical current due to their contact with an electrode surface. However, a conventional electrode surface is only a fraction of the total surface area of the entire electrochemical cell. Molecules to be measured may adsorb on a surface other than the surface of the working electrode. The result is an artificially lowered signal, which adversely affects the accuracy of the measurement. Although other applications are possible, a chemically modified surface that allows for the selective adsorption and non-adsorption of various materials such as biomolecules may be advantageously used in such a system. *See* Specification, Page 1, line 16- Page 2, line 8. A substrate according to the invention can be used in any number of devices in which selective adsorption and non-adsorption is desired. Examples of such devices include an electrochemical detection system, a chemical detection system, and an optical detection system. *See* Specification, Page 6, lines 8-12. In certain embodiments of the invention, "the coating is capable of providing a non-adsorbing surface for various materials (e.g., large biomolecules) which otherwise may possibly

be lost for electrochemical detection due to adsorption to surfaces surrounding the electrode openings." *See* Specification, Page 1, lines 6-10.

The Examiner has also asked how the invention works. *See* the Action, page 6, line 1. Applicants respectfully point out that an explanation of how an invention works is not a requirement of enablement or any other requirement of patentability. *See* M.P.E.P. § 2138.05 (quoting *Parker v. Frilette*, 462 F.2d 544, 547, 174 USPQ 321, 324 (CCPA 1972) ("[an] inventor need not understand precisely why his invention works in order to achieve an actual reduction to practice")).

As long as the specification discloses at least one method for making and using the claimed invention that bears a reasonable correlation to the entire scope of the claim, then the enablement requirement is satisfied. M.P.E.P. § 2164.01(b) (citing *In re Fisher*, 427 F.2d 833, 839, 166 U.S.P.Q. 18, 24 (C.C.P.A. 1970)). In light of the examples of enabling description above, Applicants respectfully request that the Examiner remove all rejections under § 112, first paragraph.

III. Claim Rejections under 35 U.S.C. § 102

Claims 1-30 stand rejected as being anticipated by Thorp under 35 U.S.C. § 102(b). Claims 31 and 32 have been deleted.

Applicants respectfully submit that Thorp does not teach or suggest a substrate according to the present invention. Specifically, Thorp does not teach or suggest a coating comprising a chemically crosslinked material as recited in Claim 1 that is terminated with at least one electrophilic or nucleophilic group for the adsorption and non-adsorption of biomolecules.

The Action appears to equate the oligonucleotide disclosed in Thorp with the electrophilic or nucleophilic group of the present invention. Thorp discloses an oligonucleotide probe containing a sequence complementary to a target oligonucleotide. The oligonucleotide probe is attached to a polymer membrane in contact with a conductive working surface of a nonconductive substrate. If the target hybridizes with the oligonucleotide probe, the target's guanines are detected electrochemically. *See* col. 3, lines 27-32. Thus, the oligonucleotide, as disclosed in Thorp, is a type of complementary nucleic acid that specifically binds to another nucleic acid to form a hybridized nucleic acid. The oligonucleotide in Thorp must possess a sequence, at least a portion of which is complementary to a known portion

of the sequence of the target nucleic acid. *See* col. 8, line 46-49. Thorp teaches an oligonucleotide probe that is comprised of between about 4 or 6 bases up to about 80 or 100 bases or more, more preferably between about 8 and about 30 bases. See col. 7, line 65 – col. 8, line 2.

Applicant's invention is directed to a crosslinked material that is terminated with at least one electrophilic or nucleophilic group for adsorption or nonadsorption of biomolecules. Adsorption is defined by McGraw-Hill's Dictionary of Scientific and Technical Terms, 3rd Ed. (1984) as "the surface retention of solid, liquid, or gas molecules, atoms, or ions by a solid or liquid, as opposed to absorption, the penetration of substances into the bulk of the solid or liquid." Adsorption is an electrostatic phenomenon and does not involve a formation of chemical bonds. Thus, adsorption does not involve the specific binding of complementary nucleic acids as disclosed in Thorp. As defined in the specification, an electrophilic functional group is simply a functional group having an electropositive polarity. See page 4, line 25-26. Likewise, a nucleophilic functional group is defined in the specification as a group capable of donating a pair of electrons to an electrophile. See page 5, line 18. It is believed that a positive polarity is then present on the coating surface that electrostatically attracts and adsorbs negatively charged groups. See page 5, line 7-9. Conversely, such a surface is nonadsorbing with respect to positively charged groups. Naturally, the nonadsorption of positively charged groups and adsorption of negatively charged groups would be observed when the coating is terminated with an electrophilic functional group.

The Examiner has taken the position that the electrophilic group is disclosed in Thorp at column 6, lines 10-14, which reads as follows:

> The polymer layer is preferably modified, for example, by oxidation and/or by binding thereto any conventional coupling agent such as carbondiimide, or to such agents as N-hydroxysuccinimide, glutaraldehyde, His tags, or avidin-biotin binding, in accordance with known techniques. (emphasis added).

The agents are described specifically as coupling agents, and as such, would form chemical bonds with other molecules, such as large biomolecules. In contrast, Applicant's invention includes an electrophilic or nucleophilic functional group for

use in the adsorption and non-adsorption of biomolecules. That is, Applicant's invention involves the electrostatic adsorption or non-adsorption of molecules, and chemical bonds are not form.

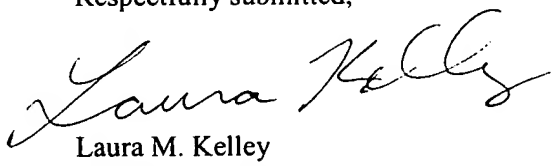
Furthermore, a coating according to the present invention may be deposited on a surface using a plasma treatment. As would be understood by those of skill in the art, a plasma treatment can only be used with small molecules because the plasma treatment process breaks down larger molecules, such as the oligonucleotides disclosed in Thorp. The coupling agents described in Thorp would break down in a plasma and could not be applied with a plasma treatment. In contrast with Thorp, which teaches an oligonucleotide probe having at least 4 or 6 bases, the electrophilic and nucleophilic functional group according to the present invention may be applied with a plasma treatment and is sized accordingly. For example, an electrophilic and nucleophilic functional group applied with a plasma treatment may be between about one and about five atoms in size.

In certain embodiments, the chemically crosslinked material includes a chemically crosslinked amorphous matrix which lacks distinct crystalline structure. *See* Specification page 4, line 10-11. Applicants submit that the polymer membrane of Thorp does not constitute an amorphous chemically crosslinked material.

IV. Conclusion

In light of the above amendments and remarks, Applicants respectfully submit that the application is in condition for allowance and respectfully requests same. The Examiner is requested to contact the undersigned to resolve any remaining issues.

Respectfully submitted,



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CERTIFICATE OF MAILING

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Commissioner for Patents, Washington, DC 20231, on April 15, 2002.

Carey Gregory

Date of Signature: April 15, 2002

VERSION WITH MARKINGS TO SHOW CHANGES MADE

The following is an addendum to the concurrently filed Amendment in response to the Official Action dated November 15, 2001 in the above-referenced application. This addendum includes a marked-up version of the changes made to the specification and claims by the present Amendment.

In the claims:

Please amend the claims as follows:

1. (Amended) A substrate for use in the adsorption and non-adsorption of biomolecules and having a **[chemically modified]** surface with at least one electrophilic or nucleophilic functional group attached thereto, said substrate **[comprising a base layer]** having a coating positioned thereon, the coating comprising a chemically crosslinked material comprising elements selected from the group consisting of (1) M, O, C, H, and N; wherein M is a metal selected from the group consisting of silicon, titanium, tantalum, germanium, boron, zirconium, aluminum, hafnium and yttrium; (2) M, O, H, and N wherein M is defined above, (3) C; (4) O, C, H, and N; and (5) M or C, and one of O, H, or N, wherein the chemically crosslinked material is terminated with the at least one electrophilic or nucleophilic functional group.

3. (Amended) The substrate according to Claim 2, wherein the chemically crosslinked material **[composition]** comprises from about 30 to about 60 percent carbon and from about 10 to about 40 percent silicon.

17. (Amended) The substrate according to Claim 1, wherein the coating has a thickness between about 200 nanometers to about 400 nanometers **[is at least a fraction of a monolayer thick.]**